

REMARKS

Claims 52, 54, 55, 83 and 87 are pending in the application. Claims 52, 55 and 87 have been amended, and as a result of the amendments to claim 55, claims 85 and 86 were rendered redundant and have been canceled. Support for the claim amendments can be found throughout the application, including the specification and the claims as originally filed. Therefore, no new matter has been added.

The claim amendments and cancellations should not be construed to be acquiescence to any of the claim rejections. Rather, the amendments and cancellations are being made solely to claim more clearly the invention, to more clearly claim the invention and to expedite prosecution of the instant application.

Applicants expressly reserve the right to prosecute the same or similar claims in subsequent patent applications claiming the benefit of priority to the instant application. 35 U.S.C. §§ 120 and 121.

Claim Rejections - 35 U.S.C. § 103

Claims 52, 54, 55, 83 and 87 stand rejected under 35 U.S.C. § 103(a) based on the Examiner's contention that they are unpatentable over German patent publication No. DE 4126543 to Kästner et al. ("Kästner"). Specifically, the Examiner asserts that it would have been obvious to one of ordinary skill in the art at the time the invention was made to follow the synthetic scheme of Kästner to make the claimed invention with a reasonable expectation of success, and that Kästner teaches compounds for the treatment of psoriasis that render the instantly claimed compounds obvious to one skilled in the art. Applicants respectfully disagree.

Kästner describes compounds that are useful for the treatment of psoriasis. The only biological data presented in Kästner show the *in vitro* inhibition of lipoxigenase by the compounds exemplified therein. See Kästner page 8. Since the compounds of the present invention are not described or claimed for the treatment of skin disorders or as lipoxigenase inhibitors, there is no nexus that relates the biological activity of the compounds of Kästner to the compounds of the present invention. The Examiner also asserts that it would have been obvious to one skilled in the art at the time the invention was made to expect the compounds of the present invention to possess the utility as taught by the compounds of Kästner. In order to find a *prima facie* case of unpatentability in instances where close or established structural

relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds, “a showing that the prior art would have suggested making the specific molecular modifications necessary to achieve the claimed invention [is] also required.” See *Takeda v. Alphapharm* (Fed. Cir. 2007), citing *In re Jones* (Fed. Cir. 1992); *In re Dillon* (Fed. Cir. 1990), *In re Grabiak* (Fed. Cir. 1985), and *In re Lalu* (Fed. Cir. 1984). “Thus, in cases involving new chemical compounds, it remains necessary to identify some reason that would have led a chemist to modify a known compound in a particular manner to establish *prima facie* obviousness of a new claimed compound” (emphasis added). See *Takeda v. Alphapharm*. Nothing in Kästner provides such a reason.

Formulae II and III of the instant claims require that ring A is substituted at the 5 position with halo. In addition, Formula II requires that ring B is trifluoromethylated at the 2 position, while Formula III requires that ring B possess a halo, CF₃, or NO₂ substituent at the 2-position. Kästner exemplifies 32 compounds, 16 of which are 5-(2-hydroxyphenyl)-3-phenylpyrazoles. Of these 16, only 3 are chlorinated at the 5 position of the 2-hydroxyphenyl. Further, not one of the compounds exemplified by Kästner are trifluoromethylated. In addition to structural similarities, the Federal Circuit has also required a showing of “‘adequate support in the prior art’ for the change in structure.” *Id.* Nothing in Kästner suggests these particular changes. Therefore, the examples of Kästner do not provide the required reasons to prepare compounds of Formulae II or III of the instant invention. Furthermore, the Examiner has not explained how Kästner suggests making the specific molecular modifications required to produce compounds of Formula II.

Nothing in Kästner provides a suggestion or motivation to prepare the compounds of the present invention. As mentioned previously, there is no nexus that relates the biological activity of the compounds of Kästner to the compounds of the present invention. Further, the vast majority of the compounds exemplified by Kästner do not possess the requisite substitution patterns required by the claims of the instant invention. For the reasons above, Applicants respectfully request the withdrawal of the rejection of claims 52, 54, 55, 83 and 87 under 35 U.S.C. § 103(a).

CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance. Applicants respectfully request that the Examiner consider the

foregoing remarks, and allow the pending claims to issue. If the Examiner believes that a telephone conference would expedite prosecution, he is invited to call the Applicants' undersigned agent or attorney.

Respectfully submitted,

/Nancy K. Brennan/

Nancy K. Brennan, Ph.D. (Reg. No. 58,990)

Agent for Applicants

Nandakumar Govindaswamy, Ph.D. (Reg. No. 56,285)

Attorney for Applicants

c/o Vertex Pharmaceuticals Incorporated

130 Waverly Street

Cambridge, MA 02139-4242

Tel.: (617) 444-6928

Fax.: (617) 444-6483